Arguments

Claims 1, 2, 4-6, 8, 9, 11, 12, 14-23, 25-27 and 29 are pending. Claims 1, 2, 4-6, 8, 9, 11, 12, 14-23, 25-27 and 29 are rejected under 35 U.S.C. § 103(a).

Claim Rejections – 35 U.S.C. § 103.

Claims 1, 2, 4-6, 8, 9, 11, 12, 14-23, 25-27 and 29 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fliri *et al.* (WO 99/09025) and Glase *et al.* (IDS) in view of Fliri *et al.* (US 5,883,094) and Faraci *et al.* (US 5,889,010).

Applicants respectfully submit that this rejection under 35 U.S.C. § 103 is in error because the combination of references does not present a *prima facie* case of obviousness of the claimed invention.

It is well established law that the PTO has the burden under 35 U.S.C. § 103 to establish a case of a *prima facie* obviousness. To satisfy this burden, an Examiner must identify both (i) a suggestion to modify a primary reference in accordance with the teachings of one or more secondary references to achieve the claimed invention and (ii) a reasonable expectation of success in making and using the modified procedure (In re Vaeck, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991)).

Moreover, an Examiner may not use an applicant's disclosure as a guide or template to select elements from prior art references which, when combined together arrive at the claimed invention (In re Fritch, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992)).

The present invention claims compounds that are *selectively active at the dopamine D4 receptor as agonists*. Said selectivity as D4 agonists is demonstrated by the *in vivo* effects in rats, in which representative compounds facilitate sexual responses in male rats.

Fliri *et al.*, (WO 99/09025) teaches indole derivative compounds that are dopamine D4 receptor agonists. Fliri et al., teaches that the compounds are useful to treat a series of disorders of the central nervous system. Applicants agree with the Examiner's assertion that Fliri *et al.*, does not teach the use of the compounds for treating sexual dysfunction (Final Office Action, page 2, point 4).

Glase *et al.*, teaches compounds with binding affinities for the dopamine D4 receptor. Glase *et al.*, teaches that the compounds are agonists of the dopamine D4 agonists receptor subtype and that may provide a useful tool in determining the contribution of D4 receptors to schizophrenia. As also recognized by the Examiner (Final Office Action, page 2, point 4), Glase *et al.*, does not teach the use of the compounds for treating sexual dysfunction.

Fliri *et al.*, (US 5,883,094) teaches several substituted benzimidazolones that have a preference for the dopamine D4 receptor. The determination of the D4 activity was performed in binding experiments using clonal cells expressing the human dopamine D4 receptor (Columns 11 and 12). Fliri *et al.*, (US 5,883,094) also teaches that the compounds of the invention possess the ability *to decrease dopamine mediated neurotransmission* in mammals, including humans (Column 9 overlapping to Column 10). Additionally, Fliri *et al.*, discloses that the compounds of the invention are allegedly useful for the treatment of a variety of conditions that can be effected or ameliorated by altering the dopamine mediated neurotransmission, including sleep disorders, sexual dysfunction, gastrointestinal disorders, psychosis, learning disorders, cardiovascular disorders, ocular disorders, Parkinson's disease, etc. Fliri *et al.*, does not provide any support for any of these indications in the exhaustive list of potential treatments. Accordingly, there is no teaching in Fliri *et al.*, to treating sexual dysfunction just as there is no teaching in Fliri *et al.*, to treating sleep disorders, sexual dysfunction, gastrointestinal disorders, psychosis, learning disorders, cardiovascular disorders, ocular disorders, Parkinson's disease, or any other of the listed disorders.

Faraci *et al.*, (US 5,889,010) teaches benzimidazoles that have D4 dopaminergic binding activity; the determination of the D4 binding activity was performed in binding experiments using clonal cells expressing the human dopamine D4 receptor (Column 22). Additionally, Faraci *et al.*, discloses that the compounds of the invention are useful for the treatment of a variety of conditions that can be effected or facilitated by altering the dopamine mediated neurotransmission. Faraci *et al.*, includes the same boilerplate language that Fliri *et al.*, used and accordingly, does not provide any teaching or suggestion to the Applicants' claimed invention

Furthermore, Fliri *et al.*, (US 5,883,094) teaches that the compounds of the invention possess the ability *to decrease dopamine mediated neurotransmission* in mammals, including humans (Column 9, line 66 to Column 10 line 4). This is tantamount to indicate that the compounds of Fliri *et al.*, are antagonists of the dopamine receptor. This alone, teaches away from the compounds in the Applicants' claimed invention.

Therefore, it appears that the Examiner is utilizing impermissible hindsight by simply selecting and combining elements from prior art references to arrive at the invention claimed in the present application.

In the "Response to the Arguments" section of the Final Office Action (in response to arguments presented by Applicants in a previous reply), the Examiner contends that the unexpected results and benefits of the compounds of the present application cannot be compared to the results obtained with apomorphine, because apomorphine is not considered prior art. The Examiner's contention is that the closest prior art are Fliri *et al.* (US 5,883,094) and Faraci *et al.*, (US 5,889,010). Applicants respectfully disagree. Neither Fliri *et al.* nor Faraci *et al.*, *disclose any effects*, neither *in vitro* nor *in vivo.* This fact *per se* makes impossible any determination that the effects obtained in the present application may or may not be superior or unexpected in view of the prior art. What the Examiner considers as the closest prior art, lacks the disclosure of any effect in any tissue, animal or disorder whatsoever. Applicants have compared the effects obtained in the present application to the effects of apomorphine, which is the dopaminergic agent most widely used to treat sexual dysfunction. As it is well know by those in close relation with the subject matter, apomorphine improves sexual responses in mammals but induces nausea and emetic effects. The representative compounds of the present application induce sexual responses in rats, without promoting an emetic effect. This alone constitute a beneficial and unexpected result over prior compounds used.

Conclusions

In view of the facts and arguments discussed above, Applicants respectfully

submit that the claims in the present application are patentable over the prior art and request allowance of the same.

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Respectfully submitted,
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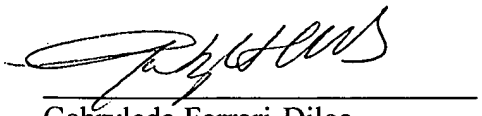

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